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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/362,598	07/28/1999	JOEL V. WEINSTOCK	3948/79934	7062
29933	7590	07/06/2007		
PALMER & DODGE, LLP KATHLEEN M. WILLIAMS 111 HUNTINGTON AVENUE BOSTON, MA 02199			EXAMINER ZEMAN, ROBERT A	
			ART UNIT 1645	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/362,598

Applicant(s)

WEINSTOCK ET AL.

Examiner

Robert A. Zeman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 April 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 24, 26 and 28-32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 24, 26 and 28-32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4-19-2007 has been entered.

Applicant's response filed on 4-19-2007 is acknowledged. Claims 24, 26 and 28-32 are pending and currently under examination.

Claim Rejections Maintained

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

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made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The instant claims are drawn to a method of screening a helminthic preparation for one or more components that reduce a Th1 immune response. The method comprises preparing and fractionating and sub-fractionating the preparation and assaying the products for the ability to reduce a Th1 immune response.

The rejection of claims 24, 26 and 28-32 under 35 U.S.C. 103(a) as being unpatentable over Kullberg et al. (Journal of Immunology, 1992, Vol. 148, No. 10, pages 3264-3270 -- IDS) is maintained for reasons of record.

Applicant argues:

1. One of skill in the art would not have been motivated to make fractions and subfractions of the *S. mansoni* preparations to produce a pure composition capable of reducing Th1 response.
2. Kullberg et al. focus on the immune response, specifically cytokine and antibody production, to an antigen in a murine *S. mansoni* model.
3. At best the teachings of Kullberg et al. may render the instant invention obvious to try.
Which is not sufficient to support a finding of obviousness.
4. Kullberg et al. already provide a working model in which to study the immune system, and does not contain teachings that would suggest to one of skill in the art to study the etiology of the mouse model itself to determine whether a component of the helminth was responsible for the changed immune response.

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5. The only guidance provided by Kullberg et al. regarding future experimentation is the implication that infected humans may have altered cell-mediated immune function to other microbial agents thus suggesting further research into concurrent infection.

Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Point 1, Kullberg et al. disclose the helminthic parasite *Schistosoma mansoni* down regulates the Th1 cytokine secretion of IL-2 and IFN- γ in mice (see abstract). Kullberg et al. further disclose that Th1 responses were determined by cytokine profiles as measured by *in vitro* ELISA assays (see materials and methods and results sections). Kullberg et al. differs from the instant invention in that they don't disclose the method steps of fractionating, sub-fractionating and testing of the sub-fractionates. However, as attested to by Drs. Weinstock and Elliot in their Declaration filed under 37 C.F.R 1.132 on 12-9-2005: "fractionation and testing of resulting fractions and sub-fractions for activity, as claimed, is a well-known and routine method for isolating the biologically active component(s) of a complex biological mixture. It is also well known in the art that the same assay can be used at each stage of a fractionation procedure to monitor which fraction(s) or sub-fraction(s) have the activity of interest" (see point 4 of Declaration). Consequently, it would have been obvious for one of ordinary skill in the art to use these "well known and routine methods" to identify the component(s) of the parasite composition responsible for the down regulation of Th1 cytokine secretion. One would have been motivated to identify said component(s) in order to produce a "pure" composition capable of reducing a Th1 response without the possible negative effects of caused by the other constituents of the nematode composition. One would have had a reasonable expectation of success since said methods are well known and routine in the art.

With regard to Points 2-4, contrary to Applicant's assertion, Kullberg et al. focuses on the **effect the helminth has** on the immune response to a non-parasitic antigen. As, Kullberg et al. observed, that the helminths altered the immune response to said antigen, it would have been obvious for the skilled artisan to determine what "component" of the helminth preparation induced said alteration. Since "fractionation and testing of resulting fractions and sub-fractions for activity, as claimed, is a well-known and routine method for isolating the biologically active component(s) of a complex biological mixture and that the same assay can be used at each stage of a fractionation procedure to monitor which fraction(s) or sub-fraction(s) have the activity of interest" (see point 4 of Declaration), it would have been obvious for one of ordinary skill in the art to use these "well known and routine methods" to identify the component(s) of the parasite composition responsible for the down regulation of Th1 cytokine secretion.

With regard to Point 5, the fact that Kullberg et al. disclose that the observed alteration in immune response could affect susceptibility to concurrent infections would not dissuade the skilled artisan from identifying the "component". The skilled artisan, even if his interest was limited to the murine model disclosed by Kullberg et al. would, as a matter of course, try to identify to agent responsible for the observed phenomena.

The rejection of claims 24, 26 and 28-32 under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (WO 96/29802 – IDS) is maintained for reasons of record.

Applicant argues:

1. One of skill in the art, given the teachings of Lee et al. would not have been motivated to perform the steps of fractionation, subfractionation and testing of the subfractions to identify an

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active component because there is not teaching or suggestion in Lee et al. to identify an active component regardless if said methods were well known in the art.

2. A showing of a suggestion or motivation to modify the teachings must be present.
3. Despite referring to the composition as an “extract”, the experiments performed by Lee et al. were done with a homogenate.
4. The homogenate was less effective than the whole worm infection, hence the skilled artisan would not have been motivated to fractionate the homogenate.
5. Given that the homogenate produced poorer results than whole nematode infection, one of skill in the art would not have had a reasonable expectation of success in identifying a component that reduced Th1 immune responses.
6. Lee et al. teach away from the combination suggested by the Office given that the homogenate was less effective than live worm infection.
7. The Office relies on the assertion that the technical know how to fractionate a sample was known in the art, however the mere fact that a device or process is known does not alone make that device or process obvious.

Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Point 1, the skilled artisan would have been motivated to identify “active component” in order to obtain a “pure” composition in order to reduce the possible deleterious effects (i.e. non-specific immune responses etc). Since said compositions are administered to allograft (transplant) patients, the skilled artisan would necessarily want to minimize unwanted immune activators.

With regard to Point 2, there does not have to be a specific suggestion within the cited art to “modify” the teachings of said cited art. The test is whether such a modification would have been obvious to one of ordinary skill in the art.

With regard to Point 3, the disclosure of Lee et al. encompasses not only homogenates, but also compositions that resulted from not only extraction methods but fractionation methods as well. Lee et al. (WO 96/29082) disclose “means for making a soluble extract are well known in the art (See, e.g., Lee et al. Immunology, 55:721, 1985)”. Lee et al. (Immunology, 55:721, 1985) disclose methods of processing tissue samples comprising enzyme digestions and fractionation. (see pages 722-723).

With regard to Points 4-6, contrary to Applicant’s assertion, the skilled artisan would not be dissuaded from identifying the active component of the “extract” since said extract was not as effective as a live worm infection. Given that the extract was shown to have efficacy the skilled artisan would be motivated to identify “active component” in order to obtain a “pure” composition in order to reduce/eliminate the possible deleterious effects (i.e. non-specific immune responses etc) associated with the live worm infection. Since said compositions are administered to allograft (transplant) patients, the skilled artisan would necessarily want to minimize unwanted immune activators.

With regard to Point 7, as Lee et al. discloses crude fractionation of its samples (see above), subfractionation of said samples in order to identify the active component would have been obvious.

As outlined previously, Lee et al. disclose the down regulation of Th1 activity in mice can be accomplished by the administration of soluble helminthic nematode extract (see page 5,

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line 21 to page 6, line 4 and page 10)). Lee et al. further disclose that Th1 responses were determined by cytokine profiles as measured by *in-vitro* ELISA assays (see Example 2). Lee et al. differs from the instant invention in that it does not explicitly disclose the method steps of fractionating, sub-fractionating and testing of the sub-fractionates. However, as attested to by Drs. Weinstock and Elliot in their Declaration filed under 37 C.F.R. 1.132 on 12-9-2005:

“fractionation and testing of resulting fractions and sub-fractions for activity, as claimed, is a well-known and routine method for isolating the biologically active component(s) of a complex biological mixture. It is also well known in the art that the same assay can be used at each stage of a fractionation procedure to monitor which fraction(s) or sub-fraction(s) have the activity of interest” (see point 4 of Declaration). Consequently, it would have been obvious for one of ordinary skill in the art to use these “well known and routine methods” to identify the component(s) of the parasite composition responsible for the down regulation of Th1 cytokine secretion. One would have been motivated to identify said component(s) in order to produce a “pure” composition capable of reducing a Th1 response without the possible negative effects of caused by the other constituents of the nematode composition. One would have had a reasonable expectation of success since said methods are well known and routine in the art.

Conclusion

No claim is allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866.

The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m...

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

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ROBERT A. ZEMAN
PRIMARY EXAMINER

July 3, 2007